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Date Submitted: January 26, 2009

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| Application Number | 10/748,410 | |
| Filing Date | 3/1/2004 | |
| First Named Inventor | Robert MARTUZA | |
| Group Art Unit | 1644 | |
| Examiner Name | Wu-Cheng Winston Shen | |
| Attorney Docket Number | 066683-0198 | |
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| U.S. PATENT DOCUMENTS | | | | | | | |
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| Examiner Cite | | U.S. Patent D | ocument | | Date of Publication of | Pages, Columns, Lines, | |
| | Number | Kind Code ² (if known) | Name of Patentee or Applicant of Cited Document | Cited Document MM-DD-YYYY | Where Relevant Passages or Relevant Figures Appear | | |
| | A1 | 5,585,096 | 1 | Martuza et al | 12/1996 | | |
| | A2 | 5,571,515 | | Scott et al. | 11/1996 | | |
| | A3 - | 6,699.468 | | Martuza et al. | 03/2004 | | |
| | A4 | 5,728,379 | | Martuza et al. | 3/1998 | | |
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| | | | | | FOREIGN PATENT DOCUMENTS | | | |
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| Examiner Cite No.1 | Cite | Foi | Foreign Patent Document | | Name of Patentee or Applicant of Cited Documents | Date of Publication of | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | |
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| | A5 | | WO 96/00 | 007 | GEORGETOWN UNIVERSITY | 01/1996 | | |
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| | | NON PATENT LITERATURE DOCUMENTS | |
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| | A6 | D'Angelica et al., "In vivo IL-2 Gene Transfection of Implanted Tumors with HSV vectors Induces a Systemic Antitumor Response," Immunobiology #3020, Proceedings of the 87 TH Ann. Mtg. of the Am. Assoc. Cancer Res, Vol. 37, (March 1996): | |
| | A7 | Toda et al., "Intratumoral Inoculation of a Replication-competent Herpes Simplex Virus, G207, Induces an Antitumor Immune Response," Pharmacology/Therapeutics (Preclinical and Clinical) #1176: Proceedings of the 88 th Ann. Mtg. of the Am. Assoc. Cancer Res., Vol. 38, (March 1997). | |
| | A8 | R.G. Vile et al., "Targeted Gene Therapy for Cancer: Herpes Simplex Virus Thymidine Kinase Gene-mediated Cell Killing Leads to Anti-Tumour Immunity That Can Be Augmented By Co-expression of Cytokines in the Tumour Cells," Biochemical Society Transactions, Vol. 25 (May 1997). | |
| | A9 | Richard G. Vile et al., "Generation of an Anti-Tumour Immune Response in a Non-immunogenic Tumour: <i>J. Cancer</i> 71 (2): 267-74 (1997). | |
| | A10 | Wanli Bi et al., "An HSVtk-mediated Local and Distant Antitumor Bystander Effect in Tumors of Head and Neck Origin in Athymic Mice," Cancer Gene Therapy, 4 (4): 246-52 (1997). | |
| | A11 | S.J. Tapscott et al., "Gene Therapy of Rat 9L Gliosarcoma Tumors By Transduction With Selectable Genes Does Not Require Drug Selection," <i>Proc. Natl. Acad. Sci.</i> , 91: 8185-89 (August 1994). | |

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| | STATEMEN | NT BY APPLIC | ANT | Filing Date | 3/1/2004 | | |
| Date Submitted: January 26, 2009 | | | | First Named Inventor | Robert MARTUZA | | |
| | Date Submitte | eu. January 2 | 6, 2009 | Group Art Unit | 1644 | | |
| | (use as many | sheets as ned | essary) | Examiner Name | Wu-Cheng Winston Shen | | |
| Sheet | 2 | of | 8 | Attorney Docket Number | 066683-0198 | | |

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| | A12 | Sin-Ichi Miyatake et al., "Defective Herpes Simplex Virus Vectors Expressing Thymidine Kinase for the Treatment of Malignant Glioma," Cancer Gene Therapy, 4 (4): 222-28 (1997). | |
| | A13 | Matthew J. During et al., "Long-Term Behavioral Recovery in Parkinsonian Rats by an HSV Vector Expressing Tyrosine Hydroxylase," <i>Science</i> , Vol. 266, (November 1994). | |
| | A14 | Peter A. Pechan et al., "A Novel 'Piggyback' Packaging System for Herpes Simplex Virus Amplicon Vectors," Human Gene Therapy 7: 2003-13 (October 1996). | |
| | A15 | Ann D. Kwong et al., "The Herpes Simplex Virus Amplicon," Virology 142: 421-25 (1985). | |
| | A16 | Pedro R. Lowenstein et al., "Herpes Simplex Virus (HSV-1) Helper Co-infection Affects the Distribution of an Amplicon Encoded Protein in Glia," <i>Molec. Neurosc.</i> , 5 (13): 1625-30 (August 1994). | |
| | A17 | Peyman Pakzaban, et al., "Effect of Exogenous Nerve Growth Factor on Neurotoxicity of and Neuronal Gene Delivery by a Herpes Simplex Amplicon Vector in the Rat Brain," <i>Human Gene Therapy</i> , 5: 987-95 (August 1994). | |
| | A18 | Howard M. Karpoff et al., "Prevention of Hepatic Tumor Metastases in Rats with Herpes Viral Vaccines and γ-Interferon," J. Clin. Invest. pp. 799-804 (February 1997). | |
| | A19 | Cindy Tung et al., "Rapid Production of Interleukin-2-Secreting Tumor Cells by Herpes Simplex Virus-Mediated Gene Transfer: Implications for Autologous Vaccine Production," <i>Human Gene Therapy</i> , 7: 2217-24 (December 1996). | |
| | A20 | Alberto L. Epstein, "HSV-1 Amplicons. Advantages and Disadvantages of a Versatile Vector System," Restorative Neurology and Neuroscience, 8: 41-43 (1995). | |
| | A21 | Alfred I. Geller et al., "An Efficient Deletion Mutant Packaging System for Defective Herpes Simplex Virus Vectors: Potential Applications to Human Gene Therapy and Neuronal Physiology," <i>Proc. Natl. Acad. Sci., USA</i> , 87: 8950-54 (November 1990). | |
| | A22 | Richard R. Spaete et al., "The Herpes Simplex Virus Amplicon: A New Eucaryotic Defective-Virus Cloning-Amplifying Vector," <i>Cell</i> , 30: 295-304 (August 1982). | |
| | A23 | F. Lim et al., "Generation of High-Titer Defective HSV-1 Vectors Using an IE 2 Deletion Mutant and Quantitative Study of Expression in Cultured Cortical Cells," <i>BioTechniques</i> , 20 (3): 460-61 (March 1996). | |
| | A24 | Giorgio Parmiani et al., "Cytokine Gene Transduction in the Immunotherapy of Cancer," Adv. Pharmacol., 40: 259-89 (1997). | |
| | A25 | J.C. Glorioso et al., "Development and Application of Herpes Simplex Virus Vectors for Human Gene Therapy," Annu. Rev. Microbiol. 49: 675-710 (1995). | |

| Examiner Signature | Date Considered | |
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| | STATEMEN | NT BY APPLICA | ANT | Filing Date | 3/1/2004 | | |
| Date Submitted: January 26, 2009 | | | c 2000 | First Named Inventor | Robert MARTUZA | | |
| | Date Submitte | eu. January 20 | 6, 2009 | Group Art Unit | 1644 | | |
| | (use as many | sheets as nec | essary) | Examiner Name | Wu-Cheng Winston Shen | | |
| Sheet | 3 | of | 8 | Attorney Docket Number | 066683-0198 | | |

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| | A26 | Alfred I. Geller, "Influence of the Helper Virus on Expression of β-Galactosidase from a Defective HSV-1 Vector, pHSVlac," J. Virol. Methods, 31: 229-38 (1991). | |
| | A27 | Alfred I. Geller et al., "A Defective HSV-1 Vector Expresses Eschirichia coli β-Galactosidase in Cultured Peripheral Neurons," Science, 241 : 1667-69 (September 1988). | |
| | A28 | Todo et al., "Treatment of Experimental Brain Tumors by Induction of Systemic Antitumor Immunity Using a Replication-Competent Herpes Simplex Virus", The 88 th Annual Meeting of American Association of Cancer Research (San Diego, CA), April 12-16, 1997. | |
| | A29 | Daniel L. Shawler et al., "Gene Therapy Appraches to Enhance Antitumor Immunity," Adv. Pharmacol., 40:309-37 (1997). | |
| | A30 | R. Martuza et al., "G207: A Multiple Deletion Herpes Mutant for Brain Tumor", J. Neuro., 82(2)377A, February 1995. | |
| | A31 | M. J. Davidson et al., "Termination of the Sequence Alteration in the DNA of the Herpes Simplex Virus Type 1 Temperature-Sensitive Mutant ts K"; J. Gen Virol. (1984), 65:859-863. | |
| | A32 | C. L. Nastala et al., "Recombinant IL-12 Administration Induces Tumor Regression in Association with IFN-γ Production", J. Immun., 153:1697-1706, August 1994. | |
| | A33 | M. Toda et al., In Situ Cancer Vaccination: An IL-12 Defective VectorAntitumor Activity", J. Immun., 160: 4457-4464, May 1998. | |
| | A34 | Restifo et al., J. Immunother. 14:182-190, (1993). | |
| | A35 | Huang et al. Science, 264:961-965, (1994). | |
| | A36 | Andreansky et al., Canc. Res., 57:1502-1509, (1997). | |
| | A37 | Qin et al. (1996) Proc. Am. Assoc. Canc. Res., Vol. 37, page 339. | |
| | A38 | Oppenheim et al., "Prospects for Cytokine and Chemokine Biotherapy", Clinical Cancer Research, Vol. 3, pp. 2682-2686, 1997 | |
| | A39 | Parmiani et al., "Cytokine Gene Transduction in the Immunotherapy of Cancer", Adv. Pharmacol., Vo. 40, pp. 259-307, 1997 | |

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Attorney Docket Number

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| | A40 | Rollins, Barrett J., "Chemokines", Blood, Vol. 90, No. 3 pp. 909-928, 1997 | |
| | A41 | Andreansky et al., "Treatment of Intracranial Gliomas in Immunocompetent Mice Using Herpes Simplex Viruses that Express Murine Interleukins", <i>Gene Therapy</i> , Vol. 5, pp. 121-130, 1998 | |
| | A42 | Hu et al., "A Phase I Study of OncoVEX ^{GM-CSF} , a Second-Generation Oncolytic Herpes Simplex Virus Expressing Granulocyte Macrophage Colony-Stimulating Factor", <i>Clinical Cancer Research</i> , Vo. 12 (22), pp. 6737-6747, 2006 | |
| | A43 | lida et al., "Protective Activity of Recombinant Cytokines Against Sendai Virus and Herpes Simplex Virus (HSV) Infections in Mice", Vaccine, Vo. 7, pp. 229-233, 1989 | |
| | A44 | Liu et al., "ICP34.5 Deleted Herpes Simplex Virus with Enhanced Oncolytic, Immune Stimulating, and Anti-Tumour Properties", <i>Gene Therapy</i> , Vo. 10, pp. 292-303, 2003 | |
| | A45 | Matsuo et al., "Interleukin-12 Protects Thermally Injured Mice from Herpes Simplex Virus Type 1 Infection", Journal of Leukoeyte Biology, Vo. 59, pp. 623-630, 1996 | |
| | A46 | Parker et al., "Engineered Herpes Simplex Virus Expressing IL-12 in the Treatment of Experimental Murine Brain Tumors", <i>PNAS</i> , Vo. 97 (5), pp. 2208-2213, 2000 | - |
| | A47 | Varghese et al., "Systemic Oncolytic Herpes Virus Therapy of Poorly Immunogenic Prostate Cancer Metastatic to Lung", Clinical Cancer Research, Vo. 12 (9), pp. 2919-2927, 2006 | |
| | A48 | Varghese et al., "Enhanced Therapeutic Efficacy of IL-12, but not GM-CSF, Expressing Oncolytic Herpes Simplex Virus for Transgenic Mouse Derived Prostate Cancers", Cancer Gene Therapy, Vo. 13, pp. 253-265, 2006 | |
| | A49 | Wong et al., "Effective Intravenous Therapy of Murine Pulmonary Metastases with an Oncolytic Herpes Virus Expressing Interleukin 12", Clinical Cancer Research, Vo. 10, pp. 251-259, 2004 | |
| | A50 | Wong et al., "Angiogenesis Inhibition by an Oncolytic Herpes Virus Expressing Interleukin 12", Clinical Cancer Research, Vo. 10, pp. 4509-4516, 2004 | |
| · | A51 | Wong et al., "Cytokine Gene Transfer Enhances Herpes Oncolytic Therapy in Murine Squamous Cell Carcinoma", Human Gene Therapy, Vo. 12, pp. 253-265, 2001 | |
| | A52 | Meignier et al., "In Vivo Behavior of Genetically Engineered Herpes Simplex Viruses R7017 and R7020: Construction and Evaluation in Rodents", <i>The Journal of Infectious Diseases</i> , Vo. 158 (3), pp. 602-614, 1988 | |
| | A53 | MEKO et al., (1995) Cancer Research, Vol. 55(1), 4765—4770. | \vdash |

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| | A54 | RAMSHAW et al., (1997) Immunological Reviews, Vol. 159, pp. 119-135. | |
| | A | | |
| | A55 | BRANSON et al., (1996) Human Gene Therapy, Vol. 7, No. 16, 1995—2002. | |
| | A56 | TODA et al., "Treatment of Human Breast Cancer in a Brain Metastatic Model by G207, a Replication Competent Multimutated herpes Simplex Virus 1", Human Gene Therapy, 9:2177-2185 (October 10, 1998). | |
| | A57 | Chahlavi et al. "Replication-Competent Herpes Simplex Virus Vector G207 and Cisplatin Combination Theapy for Head and Neck Squamous Cell Carcinoma", <i>Neoplasia</i> 1(2):162-169 (June 2, 1999) | |
| | A58 | Toda et al. "Herpes Simplex Virus as an <i>in Situ</i> Cancer Vaccine for the Induction of Specific Anti-Tumor Immunity", Human Gene Therapy 10:385-393 (February 10, 1999). | |
| | A59 | Nilaver et al. "Delivery of herpesvirus and adenovirus to nude rat intracerebral tumors after osmotic blood-brain barrier disruption", <i>Proc. Natl. Acad. Sci. USA</i> 92:9829-9833 (October 1995). | |
| | A60 | Neuwelt et al. "Delivery of ultraviolet-inactivated ³⁵ S-herpesvirus across an osmotically modified blood-brain barrier", J. Neurosurg 74:475-479 (March 1991). | |
| | A61 | Walker et al. "Local and systemic therapy of human prostate adenocarcinoma with the conditionally replicating herpes simplex virus vector G207", <i>Human Gene Therapy</i> , pages 1-28 (In Press Sept. 1999) | |
| | A62 | XO Breakefield et al. "New Biologist", 3:203-218 (1991) | |
| | A63 | MCLAUCHLAN et al., "DNA Sequence Homology Between Two Co-Linear Loci on the HSV Genome Which Have Different Transforming Abilities", THE EMBO JOURNAL, Vol. 2, 1953—1961 (1983). | |
| | A64 | SWAIN et al., "Herpes Simplex Virus Specifies Two Subunites of Ribonucleotide Reductase Encoded by 3'-Coterminal Transcripts", Journal of Virology, Vol. 57: 802—808 (1986). | |
| | A65 | DUTIA, "Ribonucleotide Reductase Induced by Herpes Simplex virus Has a Virus-Specified Constituent", J. Gen. Virol., Vol. 64:513—521, (1983). | |
| | A66 | MCLAUCHLAN et al., "Organization of the Herpes Simplex Virus Type 1 Transcription Unit Encoding Two Early Proteins With Molecular Weights of 140,000 and 40,000", J. Gen. Virol., Vol. 64:997—1006 (1983). | |

| Examiner | Date |
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| | A67 | MCGEOCH et al., "Comparative Sequence Analysis of the Long Repeat Regions and Adjoining Parts of the Long Unique Regions in the Genomes of Herpes Simplex Viruses Types 1 and 2", Journal of General Virology, Vol. 72: 3057—3075 (1991). | |
| | A68 | PERRY et al., "DNA Sequences of the Long Repeat Region and Adjoining Parts of the Long Unique Region in the Genome of Herpes Simplex Virus Type 1", J. Gen. Virol. Vol. 69 2831-2846 (1988). | |
| | A69 | JACOBSON et al., "A Herpes Simplex Virus Ribonucleotide Reductase Deletion Mutant is Defective for Productive Acute and Reactivatable Latent Infections of Mice and for Replication in Mouse Cells", Virology, Vol. 173:276-283 (1989). | |
| | A70 | SZE et al., "The Herpes Simplex virus type 1 ICP6 Gene is Regulated by a "Leaky" Early Promoter", Virus Research Vol. 26:141-152, (1992). | |
| | A71 | GOLDSTEIN et al., "Herpes Simplex Virus Type 1-Induced Ribonucletide Reductase Activity is Dispensable for Virus Growth and DNA Synthesis: Isolation and Characterization of an ICP6 lacZ Insertion Mutant", Journal of Virology, Vol. 62: 196-205, (1988). | |
| | A72 | NIKAS et al., "Structural Features of Ribonucleotide Reductase", Proteins, Structures, Function and Genetics, Vol. 1: 376-384, (1986). | |
| | A73 | HUSZAR et al., "Partial Purification and Characterization of the Ribonucleotide Reductase Induced by Herpes Simplex Virus Infection of Mammalian Cells", Journal of Virology, vol. 37:580—588 (1981). | |
| | A74 | CAMERON et al., "Ribonucletide Reductase Encoded by Herpes Simplex Virus is a Determinant of the Pathogenicity of the Virus in Mice and a Valid Antiviral Target", J. Gen. Virol., vol. 69:2607-2612 (1988). | |
| | A75 | MCGEOCH et al., "Sequence Determination and Genetic Comtent of the Short Unique Region in the Genome of Herpes Simplex Virus Type 1", J. Mol. Biol. Vol. 181:1-13 (1985). | |
| | A76 | MCGEOCH et al., "Complete DNA Sequence of the Short Repeat Region in the Genome of Herpes Simplex Virus Type 1", Nucleic Acids Research Vol. 14:1727-1745, (1988). | 7 |
| | A77 | MCGEOCH et al., "The Complete DNA Sequence of the Long Unique Region in the Genome of Herpes Simplex Virus Type 1", J. Gen. Virol. Vol. 69: 1531-1574, (1988). | |
| | A78 | MCKIE et al., "Characterization of the Herpes Simplex Virus Type 1 Strain 17+ Neurovirulence Gene RL1 and Its Expression in a Bacterial System", the Journal of General Virology, Vol. 75:733-741 (1994). | |
| | A79 | CHOU et al., "The Herpes Simplex Virus 1 Gene for ICP34.5. Which Maps in Inverted Repeats Is Conserved in Several Limited Passage Isolated but not in Strain 17syn+", Journal of Virology, Vol. 64:1014-1020 (1990). | |

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| | INFORMA' | TION DISCLOS | SURE | Application Number | 10/748,410 |
| | STATEME | NT BY APPLIC | ANT | Filing Date | 3/1/2004 |
| Date Submitted: January 26, 2009 | | | | First Named Inventor | Robert MARTUZA |
| | | | | Group Art Unit | 1644 |
| (use as many sheets as necessary) | | | essary) | Examiner Name | Wu-Cheng Winston Shen |
| Sheet | 7 | of | 8 | Attorney Docket Number | 066683-0198 |

| | | NON PATENT LITERATURE DOCUMENTS | |
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| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ |
| | A80 | ROIZMAN et al., "Genetic Engineering of Novel Genomes of Large DNA Viruses", Science, Vol. 229:1208-1214 (1985). | |
| | A81 | GOODMAN et al., "Identification, Transfer, and Characterization of Cloned Herpes Simplex Virus Invasiveness Regions", Journal of Virology, Vol. 63:1153-1161 (1989). | |
| | A82 | CHOU et al., "The Terminal of Sequence of the Herpes Simplex virus Genome Contains the Promoter of a Gene Located in the Repeat Sequences of the L Component", Journal of Virology, Vol. 57:629-637 (1986). | |
| | A83 | BOLOVAN et al., "ICP34.5 Mutants of Herpes Simplex Virus Type 1 Strain 17syn+ Are Attenuated for Neurovirulence in Mice and for Replication in Confluent Primary Mouse Embryo Cell Cultures", Journal of Virology Vol. 68:48-55 (1994). | |
| | A84 | CHOU et al., "The y,34.5 Gene of Herpes Simplex Virus 1 Precludes Neuroblastoma Cells from Triggering Total Shutoff of the Protein Synthesis Characteristic of Programmed Cell Death in Neuronal Cells", Proc. Natl. Acad. Sci. USA Vol. 89:3266—3270 (1992). | |
| | A85 | Bernard MOSS, "Genetically engineered poxvirus for recombinant gene expression, vaccination and safety", Proc Natl Acad Sci USA, Vol. 93. pp. 11341-11348, October 1996. | |
| | A86 | Stephen H. THORNE et al., "The Use of Oncolytic Vaccinia Viruses in the Treatment of Cancer: A New Role for an Old Ally?", Current Gene Therapy, 2005, 5; 429-443. | |
| | A87 | David BARBA et al., "Development of anti-tumor immunity following thymidine kinase-mediated killing of experimental brain tumors", Proc. Natl. Acad. Sci. USA vol. 91, pp. 4348-4352, May 1994. | |
| | A88 | Robert M. BERMAN et al., "Systemic Administration of Cellular IL-10 Induces an Effective Specific and Long-Lived Immune Response Against Established Tumors in Mice", The Journal of Immunology 1996, 157:231-238. | - |
| | A89 . | Mario P. COLOMBO et al., "Immunotherapy I: Cytokine gene transfer strategies", Cancer and Metastasis Reviews 16: 421-432,1997. | |
| | A90 | Jan Bubenik , "CYTOKINE GENE-MODIFIED VACCINES IN THE THERAPY OF CANCER", PHARMACOL. THER. VOL. 69, NO. 1, PP. 1-14, 1996. | |
| | A91 | Andreas MACKENSEN et al., "Immunostimulatory Cytokines in Somatic Cells and Gene Therapy of Cancer", Cytokine and Growth Factor Reviews Vol. 8, No. 2, pp. 119-128, 1997. | |
| | A92 | Jie WANG et al., "PARADOXICAL EFFECT OF GM-CSF GENE TRANSFER OF THE TUMORIGENICITY AND IMMUNOGENICITY OF MURINE TUMORS", Int. J. Cancer: 75, 459-466 (1998). | |

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| | INFORMATION D | ISCLOS | URE | Application Number | 10/748,410 | | |
| | STATEMENT BY | APPLICA | ANT | Filing Date | 3/1/2004 | • | |
| | Data Submittade Ian | | . 2000 | First Named Inventor | Robert MARTUZA | | |
| Date Submitted: January 26, 2009 | | Group Art Unit | 1644 | | | | |
| | (use as many sheets | s as nec | essary) | Examiner Name | Wu-Cheng Winston Shen | | |
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| | A93 | N. N. SENZER et al., "PHASE II CLINICAL TRIAL WITH SECOND GENERATION, GM-CSF ENCODING, ONCOLYTIC HERPESVIRUS IN UNRESECTABLE METASTATIC MELANOMA", J. CLIN. ONCOL. 26:2008 (MAY 20 SUPPL: ABSTR 9008). | |
| | A94 | Tracy HAMPTON PhD, "TARGETED CANCER THERAPIES LAGGING", JAMA, OCTOBER 25, 2006, VOL. 296, NO. 16, PP. 1951—1952. | |
| | A95 | Kaitlyn J. KELLY, "HERPES SIMPLEX VIRUS NV1020 AS A NOVEL AND PROMISING THERAPY FOR HEPATIC MALIGNANCY", Expert. Opin. Investig. Drugs (2008) 17(7) pp. 1105—1113. | |
| | A96 | Hongxing QIN , "CANCER GENE THERAPY USING TUMOR CELLS INFECTED WITH RECOMBINANT VACCINIA VIRUS EXPRESSING GM-CSF", HUMAN GENE THERAPY 7:1853-1860 (OCTOBER 1, 1996). | |
| | A97 | Joany CHOU et al., "Mapping of Herpes Simplex Virus-1 Neurovirulence to y134.5, a Gene Nonessential for Growth in Culture", SCIENCE, Vol. 250, November 30, 1990, pp. 1262—1188. | |
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